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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/520,130	03/07/2000	Robert Arathoon	P1099R2	1353
23552	7590	11/16/2004	EXAMINER	
MERCHANT & GOULD PC P.O. BOX 2903 MINNEAPOLIS, MN 55402-0903			HOLLERAN, ANNE L	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/520,130

Applicant(s)

ARATHOON ET AL.

Examiner

Anne Holleran

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 47-63 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 47-63 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 7/26/2004.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Claims 47-63 are pending and examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections Withdrawn:***

3. The rejection of claims 59-63 under 35 U.S.C. 103(a) as being unpatentable over Ridgway (Protein Engineering, 9: 617-621, 1996; cited in the IDS), Carter (U.S. Patent 5,807,706; issued September 15, 1998; effective filing date of March 1, 1995) or Carter (WO 96/27011; published September 1996; cited in the IDS), in view of Kostelney (Journal of Immunology, 148: 1547-1553, 1992; cited in the IDS), and further in view of Vaughan (supra) is withdrawn in view of applicants' arguments. Although Kostelney teaches the problem of heavy/light chain mispairings in methods of making bispecific antibodies, Kostelney fails to provide a suggestion to look to Vaughan, which happens to teach scFv constructs that bind different antigens but have light chains in common, because Kostelney solves the problem using another method. Thus, there is no suggestion provided in the prior art to combine the references.

#### ***Claim Rejections Maintained and New Grounds of Rejection:***

##### ***Double Patenting***

4. The provisional rejection of claims 47-63 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-51 of copending

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Application No. 09/863,693 is maintained for the reasons of record. Applicants have indicated that upon an indication of allowable subject matter, a terminal disclaimer may be filed, if appropriate.

5. The provisional rejection of claims 47-63 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39-49 of copending Application No. 09/373,403 is maintained for the reasons of record. Applicants have indicated that upon an indication of allowable subject matter, a terminal disclaimer may be filed, if appropriate.

6. The provisional rejection of claims 47-63 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/143,437 is maintained for the reasons of record. Applicants have indicated that upon an indication of allowable subject matter, a terminal disclaimer may be filed, if appropriate.

***Claim Rejections - 35 USC § 112***

7. Claims 47-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 51 and 57 are indefinite in the recitation that the multimerization domain is a C<sub>H</sub>3 domain of an antibody constant domain. It appears from the specification and from US Patent

5,807,706 that in order to form a multimerization domain a C<sub>H</sub>3 domain needs to be altered in structure (see page 10, line 20-26 of instant specification). A C<sub>H</sub>3 domain normally does not contribute to the dimerization of antibody constructs. Therefore, it is not clear how an unaltered C<sub>H</sub>3 domain may be a multimerization domain.

Claims 47 and 54 are indefinite because the claims are set forth as, in part, a bispecific antibody comprising “the first and second polypeptides dimerize...” (see element “(c)”). This rejection would be obviated by replacing the phrase “the bispecific antibody comprising:” with “wherein”, and also by deleting the word “which” from elements (a) and (b).

Claim 59 is indefinite because of the phrase in element of (a) of “common variable light chain domain”. This phrase should be changed to “common light chain variable domain” to maintain consistency with “heavy chain variable domain” and also because “the common light chain variable domain” is referred to in the “wherein” clause of the claim.

8. Claims 47-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The basis for this rejection is that the amendment to the specification to recite claims drawn to methods of making multispecific antibodies comprising binding domains, where the binding domains are made up of a heavy and light chain, and where the light chain is not the same for all of the binding domains is not supported by the specification. Therefore, the

recitation of claim 30 “where the light chains of the first and additional polypeptides each have three CDR regions, and have at least 98% sequence identity and only differ from one another at amino acid positions outside of the CDR regions” is not supported by the specification as originally filed. The specification teaches methods of making multispecific antibodies, where each of the binding domains comprises a “common light chain”. The specification defines “common light chain” or “common amino acid sequence of the light chain” on page 21, and as an amino acid sequence of *the* light chain in the multispecific antibody. There does not appear to be any contemplation of multispecific antibodies comprising more than one light chain (i.e., there appears to be only the contemplation that the same light chain is used for all of the binding domains present in the multispecific antibody). Even a difference of 1 amino acid between the two light chains results in a bispecific antibody having two different light chains, and there is no support in the specification that demonstrates that applicant conceived of a method of making multispecific antibodies having two different light chains. Other instances in the specification that indicate that applicant conceived of methods of making bispecific antibodies where all of the binding domains comprise a light chain having the same sequence is found at page 13, lines 14-21; page 22, line 15 – page 23, line 12; page 27, lines 2-5; page 56, lines 10-26; page 95, lines 25-28; and page 104, line 22 – page 105, line 26.

Applicants have pointed to passages (page 97-98) in the specification and assert that these passages provide support for the concept of multispecific antibodies comprising light chains where the light chains have at least 98% sequence identity to each other and only differ from one another at amino acid positions outside the CDR regions. However, this teaching of the specification appears to be directed to the process of selecting a light chain that will be used

in the process of making a multispecific antibody (i.e. selecting a common light chain). The teachings on page 97 of the specification do not provide support for bispecific antibodies having two different light chains, but instead are directed to a process for identifying one light chain that may be useful in making a bispecific antibody. Applicant is reminded that the description requirement is severable from the enablement requirement.

9. Claims 59 and 61-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The basis for this rejection is that the addition of claims 59 and 61-63, which are drawn to methods of making multispecific antibodies where the first and additional polypeptides each comprise a binding domain, the binding domains comprising a heavy chain and a common light chain, where the common light chain of the first and additional polypeptides has at least 98% sequence identity to each light chain of a first antibody and at least one additional antibody is not supported in the specification. The passages pointed to by applicant include the finding that the differences between the sequences of the compared light chains occurs outside the CDRs. This limitation is not present in the claims and the lack of this limitation is a broadening of scope that was not originally contemplated when the application was filed.

***Conclusion***

No claim is allowed.

Claims 47-63 are free of the prior art.

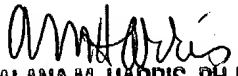
Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833.

Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran  
Patent Examiner  
November 8, 2004

  
ALANA M. HARRIS, PH.D.  
PRIMARY EXAMINER  
11/15/2004